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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,241	08/05/2003	Zhen Zhang	58369 (71699)	6657

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EXAMINER	
MILLER, MARINA I	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/635,241	ZHANG ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-111* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/27/04;10/12/04;4/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5,020.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,6,7,10,11,13-16,21,22,24-26,33,41-43,46,47,49-52,57,58,60-62,68,80,82,83,87,88,90-93,98,99,101-103 and 109.

Continuation of Disposition of Claims: Claims rejected are 1-3,5,8,9,12,17-20,23-25,27-32,34-38,40,44,45,48,53-56,59-61,63-67,69-79,81,85,86,89,94-97,100-102,104-108,110 and 111.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of various species, as follows, in the reply filed 4/1/2005 is acknowledged.

Applicant elected the following species:

A) a supervised learning algorithm, recited in claims 3, 38, and 79.

B) a support vector machine training analysis, recited in claims 5, 40, and 81.

C) presence of disease from a biological state class, recited in claims 12, 48, and 89.

D) presence of disease from a candidate biomarker group, recited in claims 17, 53, and 94.

E) a protein component, recited in claims 19, 55, and 96.

F) a protein expression profile assay, recited in claims 23, 59, and 100.

G) a protein binding partner, recited in claims 29, 65, and 106.

H) SELDI assay to measure level of data elements, recited in claims 32, 67, and 108.

Examiner's search has shown that prior art discloses different expression profiling assays comprising mass spectrometry and specifically, SELDI. Therefore, the species of mass spectrometry (recited in claims 24, 60, and 101) and SELDI expression analysis (recited in claims 25, 61, and 102) are rejoined with the elected species of expression profiling assay comprising measuring the amount and/or form of a protein (recited in claims 23, 59, and 100). However, the election requirement for other species in Species F, *i.e.*, the expression profiling

assay measuring the amount and/or form of a nucleic acid, DNA, and a carbohydrate, is maintained.

Claims 4, 6-7, 10-11, 13-16, 21-22, 26, 33, 41-43, 46-47, 49-52, 57-58, 62, 68, 80, 82-83, 87-88, 90-93, 98-99, 103, and 109 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claims.

An action on the merits of claims 1-3, 5, 8-9, 12, 17-20, 23-25, 27-32, 34-38, 40, 44-45, 48, 53-56, 59-61, 63-67, 69-79, 81, 85-86, 89, 94-97, 100-102, 104-108, and 110-111, as they read on the elected species, follows.

Information Disclosure Statement

Information Disclosure Statements (IDS) filed 8/27/2004, 10/12/2004, and 4/11/2005 have been considered by the examiner.

Specification

Abstract

The abstract is objected to because it does not properly describe the claimed invention, which is directed to a process. Applicant is required to submit a new abstract reflecting what is the essence of the claimed invention and set forth a process of the invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27, 63, and 104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27, 63, and 104 recite "data points relating to the cellular localization of components in a sample." It is not clear what limitation is intended by the applicant: (1) intracellular localization, *e.g.*, a cell membrane, cytoplasm, mitochondria, Golgi apparatus, etc.; or (2) localization pertaining to an extra cellular fraction when cells are not destroyed, or (3) localization pertaining to different cell fractions after cells are lysed (*e.g.*, membrane and cytoplasmic fractions, which may be located in the precipitate or in solution), or (4) localization pertaining to different blood cells (*e.g*, leukocytes, lymphocyte, etc.). Thus, claims 27, 63, and 104 are indefinite.

Claim Rejections - 35 USC § 101

Non-Statutory Subject Metter

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 5, 8-9, 12, 17-20, 23-25, 27, 31-32, and 34-35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-3, 5, 8-9, 12, 17-20, 23-25, 27, 31-32, and 34-35 are directed to a process for selecting an intersection subset of data elements wherein data sets comprise a plurality of forms of biological state classes. In the absence of physical steps or a transformation of a dataset by the disclosed algorithm into another essentially different set of data, the claimed method as a whole

must accomplish a practical application, *i.e.*, the method must produce a "useful, concrete and tangible result." *See* MPEP § 2106. The result of the instant method is an intersection subset of data selected from initial subsets representing biological state classes described in the specification, and therefore the result of the instant method is concrete. However, the result is not in the tangible form useful to a user because the result is not exported from a computer to the user. Thus, the instant method as a whole does not produce a concrete, tangible, and useful result, and therefore is not statutory.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-2, 8-9, 12, 17-20, 23-25, 27-28, 30-32, and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Petricoin, *The Lancet*, 359:572-577 (February 16, 2002).

Petricoin discloses a method for using proteomic patterns to identify ovarian cancer. The method comprises a step of providing wherein (i) data sets comprising plurality of biological state classes (diseases individuals v. non-affected individuals (control males and females); (ii) data sets comprise plurality of data points (each control and diseased individual); (iii) data points comprise data elements characterized by value (proteomic data measured on a protein chip by mass spectrometry) (see p. 573 and fig. 1 for the method steps). The method further comprises steps of qualifying common data elements independently for each dataset, selecting an initial subset of data (training population for comparison, p. 576, right col.), and selecting a subset from

the initial subset (see section Analytical Procedure on p. 575). Thus, Petricoin anticipates claim 1. Petricoin discloses using the discovery data to train a learning algorithm which ranks the data elements (p. 575 and fig. 1), thus anticipating claim 2. Petricoin discloses reshuffling of the two highest rated sets to form new subset candidates (p. 575), thus anticipating claim 8. Petricoin discloses selecting candidate biomarker (CA125) and testing it on a validation data set (masked serum samples, p. 575 and p. 577), thus anticipating claim 9. Petricoin discloses a biological state is a characteristic of presence of a disease (cancer) and a biomarker is a diagnostic of a disease (CA125), thus anticipating claims 12 and 17. Petricoin teaches that values of data elements represent level of components (proteins, p. 572, right col.) in a data point sample (M/Z values determined by MS, p. 573; see also peaks on fig. 2), thus anticipating claims 18 and 19. Expression of a law-molecular-weight protein (a cancer antigen CA125) is measured by coupling serum samples with a C16 hydrophobic interaction protein chip array (an immobilized capture affinity array) and the amount of the protein is measured by SELDI-TOF mass spectrometry (p. 573, right col.). Thus, Petricoin anticipates claims 20, 23-25, 28, and 30. The sample of Petricoin is serum and data collected from serum relate to the cellular localization of components in a sample (*e.g.*, components located in a soluble cell fraction or "attached" to suspended cell membranes). (p. 573, left col.), thus Petricoin anticipates claim 27. Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds an additional step to the method (p. 575, left col.), thus anticipating claim 31 and 32. Petricoin teaches collecting samples at different locations (*e.g.*, 100 control samples were provided from NOCHDP clinic in Chicago, IL, and 17 other control samples were provided by the Simone Protective Cancer Institute in Lawrenceville, NJ, p. 572-573), thus anticipating claim 35.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin, *The Lancet*, 359:572-577 (February 16, 2002), as applied to claims 1-2, 8-9, 12, 17-20, 23-25, 27-28, 30-32, and 35 above, and in view of Golub, *Science*, 286:531-537 (Oct. 15, 1999).

Petricoin teaches the method of claims 1-2, 8-9, 12, 17-20, 23-25, 27-28, 30-32, and 35, as set forth above. Petricoin's samples were obtained from women with different subtypes of ovarian cancer from premenoposal and postmenoposal women and from women with familial breast or ovarian cancer (*i.e.*, samples were obtained from different populations) (p. 573).

Although Petricoin discloses that cases with ovarian cancer were eligible if they had had a serum banked before pathological staging by a gynecological oncologist, Petricoin does not explicitly disclose different collecting protocols.

Golub discloses a method for classifying cancer by using gene expression monitoring wherein different type of samples, bone marrow and blood, were collected by different protocols (*e.g.*, samples from SJCRH were processed with a very different protocol (p. 536-537, paragraph 23). Also, collection of bone marrow and blood requires different protocols. Golub also discloses collecting samples at different collecting sites and from different populations (p. 536-537, paragraph 23).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to use different collecting protocols for different data sets, as taught by Golub, where the motivation would have been to use different type of tissues for constructing a model predictive of cancer for unknown samples, as taught by Golub, (p. 532, left col.).

Claims 3, 5, 29, 36-38, 40, 44-45, 48, 53-56, 59-61, 63-67, 71-79, 81, 85-86, 89, 94-97, 100-102, and 104-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin, *The Lancet*, 359:572-577 (February 16, 2002), as applied to claims 1-2, 8-9, 12, 17-20, 23-25, 27-28, 30-32, and 35 above, and in view of Barnhill, U.S. Patent 6,789,069.

Claims 3 and 5 limit claims 1 and 2 to a supervised learning algorithm and specifically, a support vector machine analysis. Claim 29 limits claims 1, 18, 20, and 28 to a protein binding partner. Claims 36-38, 40, 44-45, 48, 53-56, 59-61, and 63-67 are directed to a computer readable medium capable of executing the instant method. Claims 71-79, 81, 85-86, 89, 94-97, 100-102, and 104-108 are directed to a computer system.

Petricoin teaches the method of claims 1-2, 8-9, 12, 17-20, 23-25, 27-28, 30-32, and 35, as set forth above. Petricoin also discloses using mass spectrometry (*i.e.*, SELDI) for acquiring and processing experimental data and bioinformatics software for processing data (p. 573 and 575). Petricoin discloses a computer based chip system (the Protein Biology System 2 SELDI-TOF mass spectrometer such as Ciphergen Biosystems with a detector and a chip reader, p. 573). Petricoin also discloses that data were collected and were used later for analysis (*i.e.*, data are stored).

Petricoin does not teach a supervised learning algorithm and specifically, a support vector machine analysis. Petricoin does not disclose protein binding partners in an expression profiling assay. Petricoin does not teach a computer system and a computer readable medium for performing the method of Petricoin.

Barnhill discloses a method for classifying unknown samples using a learning machine, similar to that of Petricoin. Barnhill discloses different methods for data acquisition such as nucleic acid arrays and protein expression assays (*e.g.*, antibody chips to identify specific proteins, col. 13, line 5-15). Barnhill method comprises acquiring expression data and processing data via creating training set by using a support vector machine and using the set to classify unknown data (col. 5, line 1-54). Barnhill discloses a gene chip, a mass spectrometer, and a protein binding assay comprising a protein binding partner (col, 1-2 and col. 13, line 5-15).

Barnhill discloses a computer system and a program for executing his method wherein data are entered into a computer system via a user interface (col. 22, line 27-67 and fig. 10-12), qualified, and selected (*see* for a general description of a computer system and programs col. 21, line 27 – col. 26, line 38 and fig. 10-12). The system comprises a processor, an input device, a memory, programs, and a network connector (fig. 10). Example 1 illustrates the method and the system for executing the method of Barnhill wherein tables 2-4 represent a database of ranked data obtained during the execution of the method (col. 38-42).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to use a supervised learning algorithm and specifically, a support vector machine analysis, as taught by Barnhill, where the motivation would have been to improve pre- and post-processing data and maximize the value of genomic and proteomic information, as

taught by Barnhill, col. 4, line 29-33. It would further have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to use a protein expression assay, as taught by Barnhill, where the motivation would have been to determine efficiently specific proteins from a large protein expression pool, as taught by Barnhill (col. 12, line 10 – col. 13, line 15). It would have also been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to use a computer and a computer readable medium for executing Petricoin's method, as taught by Barnhill, where the motivation would have been to manage large amount of complicated data in genomic and proteomic investigations, as taught by Barnhill, col. 1-2.

Claims 69-70 and 110-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin, *The Lancet*, 359:572-577 (February 16, 2002), in view of Barnhill, U.S. Patent 6,789,069, as applied to claims 1-3, 5, 8-9, 12, 17-20, 23-25, 27-29, 30-32, 35-38, 40, 44-45, 48, 53-56, 59-61, 63-67, 71-79, 81, 85-86, 89, 94-97, 100-102, and 104-108 above, and further in view of Golub, *Science*, 286:531-537 (Oct. 15, 1999).

Claims 69-70 are directed to a computer readable medium capable of executing the instant method. Claims 110-111 are directed to a computer system.

Petricoin and Barnhill teach and make obvious claims 1-3, 5, 8-9, 12, 17-20, 23-25, 27-29, 30-32, 35-38, 40, 44-45, 48, 53-56, 59-61, 63-67, 71-79, 81, 85-86, 89, 94-97, 100-102, and 104-108, as set forth above. Petricoin teaches collecting samples at different locations (*e.g.*, 100 control samples were provided from NOCHDP clinic in Chicago, IL, and 17 other control samples were provided by the Simone Protective Cancer Institute in Lawrenceville, NJ, p. 572-

573). The samples were obtained form women with different subtypes of ovarian cancer from premenoposal and postmenoposal women and from women with familial breast or ovarian cancer (*i.e.*, samples were obtained from different populations) (p. 573). Barnhill teaches that samples may be collected from one or more local and remote sources (col. 14, line 3-5).

Although Petricoin discloses that cases with ovarian cancer were eligible if they had had a serum banked before pathological staging by a gynecological oncologist, Petricoin and Barnhill do not explicitly disclose different collecting protocols.

Golub discloses a method for classifying cancer by using gene expression monitoring wherein different type of samples, bone marrow and blood, were collected by different protocols (*e.g.*, samples from SJCRH were processed with a very different protocol (p. 536-537, paragraph 23). Also, to collect bone marrow and blood one has to use different collecting protocols. Golub also discloses collecting samples at different collecting sites and from different populations (p. 536-537, paragraph 23).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Barnhill to uses different collecting protocols for different data sets, as taught by Golub, where the motivation would have been to use different type of tissues for constructing a model predictive of cancer for unknown samples, as taught by Golub, (p. 532, left col.).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph. D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marina Miller
Examiner
Art Unit 1631

MM

MARJORIE A. MORAN
PRIMARY EXAMINER

5/9/05